

DATE: Wednesday, February 12, 2003

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<u>Set</u>	<u>Name</u>	Query
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side by side

L1	htra or htr-a	81	L1
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DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=AND

=AND			
L2	htra or htr-a	143	L2
L3	(L2 or 11) and (dna or cdna or vector or rna or mrna or coding or encode or encodes or encoding or nucleic or nucleotide or nuclear or pcr)	137	L3
L4	(L2 or 11) same (dna or cdna or vector or rna or mrna or coding or encode or encodes or encoding or nucleic or nucleotide or nuclear or pcr)	69	L4
L5	L4.clm.	3	L5
L6	(L2 or 11) same (gene or genetic or genetically or dna or cdna or vector or rna or mrna or coding or encode or encodes or encoding or nucleic or nucleotide or nuclear or pcr)	96	L6
L7	L6.clm.	7	L7
L8	L7 not 15	4	L8
L9	L6.ti,ab. not 17	10	L9
L10	arob.clm. or aro-b.clm.	10	L10
L11	curtiss\$.in. and aro\$5	98	L11
L12	L11 and (attenuat\$ or mutant or mutation or mutagenesis)	14	L12



L13	L12 and ((a near d) or a-d)	11	L13
L14	aro near a-d	0	L14
L15	aro near3 a-d	0	L15
L16	aroa-d	0	L16
L17	a near b near c near d	64682	L17
L18	aro near5 (a near b near c near d)	0	L18
L19	do-like	1	L19
L20	(do-like) near10 (proteinase or protease or peptidase)	0	L20
L21	(do-like) same (proteinase or protease or peptidase)	0	L21
L22	serine near5 (proteinase or protease or peptidase)near10 temperature	54	L22
L23	L22 and (gene or genetic or genetically or dna or cdna or vector or rna or mrna or coding or encode or encodes or encoding or nucleic or nucleotide or nuclear or pcr)	40	L23
L24	L22 same(gene or genetic or genetically or dna or cdna or vector or rna or mrna or coding or encode or encodes or encoding or nucleic or nucleotide or nuclear or pcr)	5	L24
L25	serine near5 (proteinase or protease or peptidase)	7447	L25
L26	L25.ti,ab,clm.	2346	L26
L27	L26 same(gene or genetic or genetically or dna or cdna or vector or rna or mrna or coding or encode or encodes or encoding or nucleic or nucleotide or nuclear or pcr).ti,ab,clm.	522	L27
L28	L27 and (salmonella or coli or bacillus or pseudomonas or haemophilus or influenzae or campylobacter or helicobacter or brucella or	197	L28



	chlamydia or bartonella or yersinia or escherichia)		
	L27 same (salmonella or coli or bacillus or pseudomonas or haemophilus or influenzae or		
L29	campylobacter or helicobacter or brucella or chlamydia or bartonella or yersinia or escherichia).ti,ab,clm.	48	L29
L30	125 same (12 or htr)	32	L30

END OF SEARCH HISTORY

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L30: Entry 22 of 32

File: USPT

Dec 21, 1999

DOCUMENT-IDENTIFIER: US 6004794 A

TITLE: Human serine protease

Detailed Description Text (2):

As used herein, the term "PSP1 polynucleotide" or "PSP1" refers to DNA molecules comprising a nucleotide sequence that encodes PSP1 and alternative splice variants, i.e., homologs and isoforms, and polymorphic variants. PSP1 binds to a region encompassing amino acids 269-413 of the human PS-1 protein, contains a conserved serine protease motif and exhibits homology to the E. coli serine protease htrA described by Lipinska et al. in Nucl. Acids Res. 16, 10053-10066 (1988) and a putative human serine protease with an IGF-binding motif (Ohno, I., et al., Genbank Accession No. D87258 (1996)), hereinafter referred to as D87258.

Detailed Description Text (90):

The AD fusion plasmids were subjected to restriction digest analysis and sequencing as indicated above. Sequence analysis of one of the interacting fusion protein cDNAs revealed a 519 nucleotide open reading frame (SEQ ID NO: 1) encoding a 173 amino acid (SEQ ID NO: 2) protein starting with an GGA at position 2 and terminating with a TGA at position 523 of SEQ ID NO: 1. GenBank searches using the BLASTX and BLASTN algorithms with the cDNA sequence or with the deduced amino acid sequence indicated homology to a portion of the E. coli serine protease htrA described by Lipinska et al., supra, (SEQ ID NOs: 13 and 14). This novel cDNA was designated PSP1.

<u>Detailed Description Text</u> (95):

Alignment of the deduced amino acid sequence of PSP1-1 (SEQ ID NO: 25) to E. coli https://h



Ser-197 and may be deleted or replaced by alanine. Accordingly, the present invention provides analogs of Hin47 protein having decreased protease activity due to single or multiple amino acid deletions, replacements or additions within the Hin47 protein.

Detailed Description Text (9):

As discussed above, Hin47 shows homology with E coli <a href="https://html.nc.nlm.nc.n

Detailed Description Text (61):

The deduced amino acid sequence of Hin47 protein determined in Example 2 above was compared with all other known proteins in the Genbank data base. As described above, Hin47 protein is described in published PCT applications WO 94/00149, WO 92/11367 and WO 92/10936 to be an adhesin molecule of Haemophilus. It was, therefore, a surprising and unexpected discovery of the present invention that Hin47 protein has significant amino acid homology (55%) with the <u>serine proteases</u> E. coli <a href="https://doi.org/10.1001/journal.org/10.1001/journa

<u>Detailed Description Text</u> (64):

As explained above, H. influenzae Hin 47, E. coli <a href="https://htt

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L30: Entry 17 of 32

File: USPT

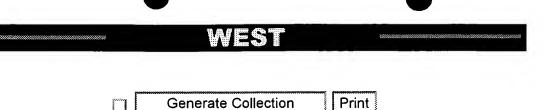
Nov 28, 2000

DOCUMENT-IDENTIFIER: US 6153580 A

TITLE: Analog of haemophilus Hin47 with reduced protease activity

Detailed Description Text (8):

Referring to FIG. 1, there is illustrated restriction maps of plasmids JB-1031-1-14 and JB-1068-2-2 that contain a portion encoding Hin47 protein from non-typable H. influenzae SB33. The nucleotide sequence of the Hin47 gene was determined and is shown in FIG. 2 along with the deduced amino acid sequence of the Hin47 protein. Referring to FIG. 3, there is shown an amino acid sequence alignment of H. influenzae Hin47 and the serine proteases htrA from Escherichia coli and htrA from Salmonella typhimurium. This alignment for the first time reveals the unexpected discovery of the present applicants that Hin47 is related to bacterial serine proteases and that Hin47 has protease activity. Hin47 has previously been reported to be an adhesin. The discovered protease activity thereof greatly limits the usefulness of natural Hin47 as an immunogen for vaccination and as an antigen in diagnostic uses. The sequence alignment shown in FIG. 3 revealed that the htrA proteins and Hin47 contain a GNSGGAL (SEQ ID NO: 17) sequence between residues 195 and 201 of the mature protein. The consensus sequence of the active site of serine proteases is GDSGGPK (SEQ ID NO: 18) (Brenner, 1988) and the active residue is serine. Thus, Serine-197 in Hin47 was mutated to produce an analog of Hin47 reduced in protease activity, in accordance with one embodiment of the invention. In a particular embodiment, Serine-197 was replaced by alanine. Amino acid residues 57 to 256 of Hin47 were further aligned with known proteases and the active site residues identified from the local homologies surrounding the residues of the catalytic triad (FIG. 4). There is a standard numbering system for serine proteases in which the catalytic triad residues are numbered as His-57, Asp-102 and Ser-195. These correspond to residues His-91, Asp-121 and Ser-197 in the sequential numbering system. Thus, referring to FIG. 4, there is shown a structure-based alignment of ten structurally determined serine proteases (SEQ ID NOS: 7 to 16) in which homologous residues are aligned primarily on the basis of similar locations in three-dimensional space. The location of many of the residues in the hydrophobic core of Hin47, as well as residues around the active site can be aligned reasonably well to identify functional amino acids of the Hin47 protease. Thus, other amino acid residues in Hin47 that contribute to protease activity of the protein include His-91 and Asp-121. In particular embodiments, His-91 may be replaced by alanine, lysine or arginine. In an additional embodiment, Asp-121 may be replaced by alanine or glutamic acid. In an additional embodiment, Serine-197 may be replaced by alanine, serine or threonine. Although the provision of an analog of Hin47 having reduced protease activity has been exemplified herein by particular amino acid substitution within Hin47 protein, the discovery of the protease activity and the methods of Hin47 expression, purification and analysis provided herein, allow for the production of other analogs having at least one other amino -acid deleted or replaced or having at least one additional amino acid inserted into the Hin47 protein. In particular applications and embodiments, it may be desirable to simultaneously alter several amino acids of the Hin47 protein to particularly reduce the protease activity of Hin47. The multiple amino acids may be His-91 and Ser-197 and may be deleted or replaced by alanine. In an alternative embodiment, the multiple amino acids may be His-91, Asp-121 and



L30: Entry 10 of 32

File: USPT

Jul 2, 2002

DOCUMENT-IDENTIFIER: US 6413768 B1

TITLE: Expression plasmids

<u>Detailed Description Text</u> (326):

Pallen, M. J. and B. W. Wren. 1997. The HtrA family of serine proteases. Molecular Microbiology 26:209.

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L30: Entry 8 of 32

File: USPT

Dec 3, 2002

DOCUMENT-IDENTIFIER: US 6489136 B1 TITLE: Cell proliferation related genes

Brief Summary Text (132):

In preferred embodiments, the Omi polypeptide includes a <u>serine protease</u> catalytic domain similar to L56 and <u>HtrA serine protease</u> catalytic domains. Generally, the <u>serine protease</u> catalytic domain is about 312 residues, and preferably has about 50, 60, 70, 80, 90, or 95% sequence identity with the protein sequence shown in SEQ ID NO:5 (amino acid residues 217-529).

Detailed Description Text (34):

The <u>serine protease</u> catalytic domain of Omi shows extensive homology with E.coli heat shock protease, <u>HtrA</u>, as well as with a mammalian protein called L56 (Zumbrunn and Trueb FEBS Lett. 398:187-192, 1996) (FIG. 5a). No homology is found in the regulatory domains The catalytic domain of Omi has 51% identity and 68% similarity with the corresponding domain of L56, and 36% identity and 58% similarity with <u>HtrA</u>, (FIG. 5b).





Generate Collection Print

L30: Entry 9 of 32

File: USPT

Jul 23, 2002

DOCUMENT-IDENTIFIER: US 6423312 B1

TITLE: Compositions including glycosaminoglycans degrading enzymes and use of same against surface protected bacteria

Other Reference Publication (24):

Boucher et al, "Two Distinct Loci Affecting Conversion to Mucoidy Pseudomonas Aeruginosa in Cystic Fibrosis Encode Homologs of the <u>Serine Protease HtrA</u>", J. Bacteriol, 178(2):511-523, 1996)Abstract).



Generate Collection Print

L9: Entry 3 of 10

File: EPAB

Aug 3, 1995

PUB-NO: WO009520665A1

DOCUMENT-IDENTIFIER: WO 9520665 A1

TITLE: EXPRESSION OF HETEROLOGOUS PROTEINS IN ATTENUATED BACTERIA USING THE

HTRA-PROMOTERS

PUBN-DATE: August 3, 1995

INVENTOR-INFORMATION:

NAME	COUNTRY
KHAN, MOHAMMED ANJAM	GB
CHATFIELD, STEVEN NEVILLE	<i>G</i> B
LI, JINGLI	GB

ASSIGNEE-INFORMATION:

NAME	COUNTRY
MEDEVA HOLDINGS BV	NL
KHAN MOHAMMED ANJAM	GB
CHATFIELD STEVEN NEVILLE	GB
LI JINGLI	GB

APPL-NO: GB09500196

APPL-DATE: January 31, 1995

PRIORITY-DATA: GB09401795A (January 31, 1994)

INT-CL (IPC): <u>C12 N 15/62</u>; <u>C12 N 15/70</u>; <u>C12 N 15/74</u>; <u>C12 N 1/21</u>; <u>A61 K 39/08</u>

EUR-CL (EPC): C12N015/70; C12N015/74, C07K014/33, C12N015/62

ABSTRACT:

CHG DATE=19990617 STATUS=0>The invention provides a <u>DNA</u> construct comprising the <u>htrA</u> promoter sequence operably linked to a <u>DNA</u> sequence <u>encoding</u> one or more heterologous proteins, replicable expression <u>vectors</u> containing the constructs, and attenuated bacteria containing the constructs or <u>vectors</u>. The invention also provides a vaccine composition comprising an attenuated bacterium as defined above, or a fusion protein expressed from a construct as defined above, and a pharmaceutically acceptable carrier.



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L10: Entry 5 of 10

File: USPT

May 15, 2001

US-PAT-NO: 6231871

DOCUMENT-IDENTIFIER: US 6231871 B1

TITLE: Live in ovo vaccine

DATE-ISSUED: May 15, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

Print

COUNTRY

Coloe: Peter John

East Doncaster

ΑU

ASSIGNEE-INFORMATION:

NAME

CITY

STATE ZIP CODE

COUNTRY

TYPE CODE

American Cyanamid Company

Madison NJ

02

APPL-NO: 08/643718 [PALM] DATE FILED: May 6, 1996

PARENT-CASE:

RELATED APPLICATIONS This application is a continuation of U.S. application Ser. No. 08/147,207, filed Nov. 3, 1993 (now abandoned).

INT-CL: [07] A61 K 39/112, A61 K 48/00, A61 K 39/02, A01 N 63/00

US-CL-ISSUED: 424/2581; 424/932, 424/931, 424/9348, 424/2001, 424/1841, 424/826 US-CL-CURRENT: 424/258.1; 424/184.1, 424/200.1, 424/826, 424/93.1, 424/93.2, 424/93.48

FIELD-OF-SEARCH: 424/258.1, 424/93.2, 424/93.1, 424/43.48, 424/200.1, 424/184, 424/826

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected

Search ALL

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PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
<u>2851006</u>	September 1958	Taylor et al.	119/1
<u>3120834</u>	February 1964	Goldhaft et al.	119/1
<u>3256856</u>	June 1966	Nicely et al.	119/1
<u>4458630</u>	July 1984	Sharma et al.	119/1
4735801	April 1988	Stocker	424/92
<u>5206015</u>	April 1993	Cox et al.	424/93 <i>C</i>
<u>5210035</u>	May 1993	Stocker	435/1723
<u>6033670</u>	March 2000	Bublot et al.	
6048535	April 2000	Sharma	

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0 291 173 A2	November 1988	EP	
WO 85/02545	June 1985	WO	
WO 91/04749	April 1991	WO	

OTHER PUBLICATIONS

Hassan, J. O., and Curtiss, R. III, "Control of Colonization by Virulent Salmonella Typhimurium by Oral Immunization of Chickens with Avirulent .DELTA. cya .DELTA. crp S. Typhimurium", Res. Microbiol., 141:839-850 (1990).

Cooper, Gerard L., et al., "Vaccination of Chickens with Chicken-Derivedi Salmonella enteritidis phage type-4 aro-A Live Oral Salmonella Vaccines", vaccine, 10 (4):247-254 (1992).

Stocker, Bruce A.D., "Auxotrophic Salmonella typhi as Live Vaccine", Vaccine, 6:141-145 (1988).

Hoiseth, Susan K., et al., "Genes aro A and ser C of Salmonella typhimurium Constitute an Operon", Journal of Bac.,, 163 (1):355-361 (1985).

Alderton, M. R., et al., "Humoral Responses and Salmonellosis Protection in Chickens Given a

Vitamin-Dependent Salmonella Typhimurium Mutant", Aviana Diseases, 35:435-442 (1991).

Griffin, Hugh G., "Attenuated Salmonella as Live Vaccines: Prospects for Multivalent Poultry Vaccines", World's Poultry Science Journal, 47(2):129-140 (1991).

Dougan, Gordon, et al., "Construction and Characterization of Vaccine Strains of Salmonella Harboring Mutations in Two Different are Genes", The Journal of Inf. Disease, 158(6):1329-1335 (1988).

Cooper, Gerard L., et al., "Vaccination of Chickens with a Salmonella enteridtidis aroA Live Oral Salmonella Vaccine", Microbial Pathogenesis, 9:255-265 (1990).

Dougan, Gordon, et al., "Live Bacterial Vaccines and Their Application as Carriers for Foreign Antigens",

Advances in Veterinary Science and Comparitive Medicine, vol. 33, Vaccine Biotechnology, pp. 271-300 (1989).

O'Callaghan, David, et al., "Characterization of Aromatic- and Purine-Dependent Salmonella typhimurium:

Attenuation, Persistence, and Ability to Induce Protective Immunity in BALB/c Mice", Infection and Immunity,



56(2): 419-423 (1988).

O'Gaora, Peadar, et al., "Cloning and Characterisation of the serC and aroA Genes of Yersinia enterocolitica, and Construction of an aroA Mutant", Gene, 84:23-30 (1989).

Roberts, Mark, et al., "Construction and Characterization In Vivo of Bordetella pertussis aroA Mutants", Infec. and Immunity 58(3):732-739 (1990).

Bowe, Frances, et al., "Virulence, Persistence, and Immunogenicity of Yersinia enterocolitica 0:8 aro A Mutants", Infection and Immunity, 57(10):3234-3236 (1989).

Dougan, Gordon, et al., "The Genetics of Salmonella and Vaccine Development", In Biology of Salmonella, F. Cabello, et al., eds. (Plenium Press), pp. 323-332 (1993).

Schodel, florian, et al., "Construction of a Plasmid for Expression of Foreign Epitopes as Fusion Proteins with Subunit B of Escherichia coli Heat-Labile Enterotoxin", Infection and Immunity, 57(4):1347-1350 (1989). Kelly, Sandra M., et al., "Characterization and Protective Properties of Attenuated Mutants of Salmonella choleraesuis", Infection and Immunity, 60:4881-4890 (1992).

ART-UNIT: 165

PRIMARY-EXAMINER: Minnifield: Nita

ABSTRACT:

The present invention relates generally to modified microorganisms suitable for use as live in ovo vaccines for avian species. The live in ovo vaccines of the present invention are useful for inducing immunity before or immediately after hatching against a virulent form of the modified microorganism or a microorganism immunologically related to the modified microorganism or a virulent organism or virus carrying an antigenic determinant expressed by the modified microorganism in the live vaccine. The subject live in ovo vaccines are particularly efficacious in enhancing the survival rate of newly-hatched poultry birds.

26 Claims, 10 Drawing figures

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L10: Entry 5 of 10

File: USPT

May 15, 2001

DOCUMENT-IDENTIFIER: US 6231871 B1

TITLE: Live in ovo vaccine

CLAIMS:

- 8. A method according to claim 7 wherein the attenuated Salmonella microorganism carries a nucleotide substitution, deletion, insertion, or combination thereof in one or more genes selected from the group consisting of aroA, aroB, aroC and aroD.
- 9. A method according to claim 8 wherein the attenuated Salmonella microorganism carries a deletion in at least one gene selected from the group consisting of aroA, <u>aroB</u>, aroC and aroD.
- 20. A fertilized egg according to claim 19 wherein the attenuated Salmonella microorganism carries a nucleotide substitution, deletion, insertion, or combination thereof in one or more genes selected from the group consisting of aroA, aroB, aroC and aroD.
- 21. A fertilized egg according to claim 20 wherein the attenuated Salmonella microorganism carries a deletion in at least one gene selected from the group consisting of aroA, aroB, aroC and aroD.

ost is in DialUnits ?ds Items Description Set HTRA (10N) (PYLROI OR PYLORI OR PYLORIS OR PYLORIDIS OR PY-S1 25 LORUM OR HPYLORI? OR HELICOBACTER?) 15 RD (unique items) S2 ?t s2/9/13 2/9/13 (Item 1 from file: 65) DIALOG(R) File 65: Inside Conferences (c) 2003 BLDSC all rts. reserv. All rts. reserv. INSIDE CONFERENCE ITEM ID: CN004355891 00453860 Molecular Cloning and Nucleotide Sequence Determination of htrA , a Gene Encoding a 48-kDa Stress Protein of Helicobacter pylori Kleanthous, H.; Clayton, C. L.; Morgan, D. D.; Pallen, M. J. CONFERENCE: Basic and clinical aspects of helicobacter pylori infection-4th Workshop P: 195-202 New York, Springer-Verlag, c1994 ISBN: 3540567208; 0387567208 LANGUAGE: English DOCUMENT TYPE: Conference Selected papers CONFERENCE EDITOR(S): Gasbarrini, G.; Pretolani, S. CONFERENCE SPONSOR: European Helicobacter Pylori Study Group CONFERENCE LOCATION: Bologna, Italy CONFERENCE DATE: Nov 1991 (199111) (199111) BRITISH LIBRARY ITEM LOCATION: 94/09285 Basic NOTE: xii, 313 p.; Described as proceedings. See also 4588.3404 vol 23 no 9 and supp 1 2 1991 for abstracts and programme DESCRIPTORS: helicobacter pylori infection; helicobacter pylori $2 \times 10^{-7} =$

>>>KWIC option is not available in file(s): 399

OLYPEPTIDES FROM MORAXELLA (BR. HAMELLA) CATARRHALIS POLYPEPTIDES ISOLES A PARTIR DE MORAXELLA (BRANHAMELLA) CATARRHALIS

Patent Applicant/Assignee:

SMITHKLINE BEECHAM BIOLOGICALS S A,

RUELLE Jean-Louis,

Inventor(s):

RUELLE Jean-Louis,

Patent and Priority Information (Country, Number, Date):

Patent:

WO 9955871 A1 19991104

Application:

WO 99EP2764 19990420 (PCT/WO EP9902764)

Priority Application: GB 988720 19980423

Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE

ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT

LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT

UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD

RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF

CG CI CM GA GN GW ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 20977

Fulltext Availability: Detailed Description

Detailed Description

... BASBO I I of Moraxella catarrhalis, which is related by amino acid sequence homology to Helicobacterpylori HtrA polypeptide. The invention relates especially to BASBO I I having the nucleotide and amino acid...polynucleotide sequence showed significant similarity (40% identity in a 364 amino acids overlap) to the HtrA serine protease of Helicobacterpylori, as well as to the HtrA serine protease of